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ARNOLD & PORTER LLP
ATTN: IP DOCKETING DEPT.
555 TWELFTH STREET, N.W.
WASHINGTON, DC 20004-1206

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DEJONG, ERIC S	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/300,482
Filing Date: April 28, 1999
Appellant(s): CHEIKH ET AL.

Gautam Prakash
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 06/04/2007 appealing from the Office action mailed 01/04/2007.

(1) Real Party of Interest

The statement identifying by name the real party of interest contained in the brief is correct.

(2) Related Appeals and Interferences

The statement of the related appeals, interferences, and judicial proceedings contained in the brief is correct.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Attwood, T. "The Babel of Bioinformatics" Science, Vol. 290, (Oct 2000), pages 471-473.

Gerhold et al. "It's the genes! EST access to human genome content" BioEssays, Vol. 18, (1996), pages 973-98.

Wells et al. "The chemokine information source: identification and characterization of novel chemokines using the WorldWideWeb and Expressed Sequence Tag Databases", Journal of Leukocyte Biology, Vol. 61, (1997), pages 545-550.

Russell et al. "Structural Features can be Unconserved in Proteins with Similar Folds" Journal of Molecular Biology, Vol. 244, (1994), pages 332-350.

(9) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

A. Claim Rejections - 35 USC 101/112, First Paragraph

Claims 1, 11-13, 15-22, 24, 28, 30, and 31 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility. This rejection is maintained and reiterated from the Office action mailed 12/20/2000.

The claimed nucleic acids are not supported by a specific asserted utility because the disclosed use(s) of the nucleic acids are not specific and are generally applicable to any nucleic acid. The specification states that the nucleic acid compounds may be useful as probes for assisting in the isolation of full-length cDNAs or genes which would be used to make protein and optionally further usage to make the corresponding antibodies, gene mapping, isolation of homologous sequences, detection of gene expression such as in Northern blot analysis, molecular weight markers, chromosomal markers, and for numerous other generic genetic engineering usages. Similarly, protein may be used for detection of expression, antibody production, Western blots, etc. These are non-specific uses that are applicable to nucleic acid(s) and/or proteins in general and not particular or specific to the nucleic acid(s) being claimed.

Further, the claimed nucleic acids are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not currently available. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, none of the proteins that are alleged to be produced as final products resulting from processes involving the instantly claimed nucleic acid have asserted or identified specific and substantial utilities. The research contemplated by applicants to characterize potential protein products, especially

biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above and in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the compounds.

It is noted that the instant disclosure lists a number of sequences which are known in the prior art and which has a high percentage sequence similarity to a claimed sequence. Absent factual evidence, a percentage sequence similarity of less than 100% does not provide sufficient guidance or support to one skilled in the art so as to determine what biochemical activity or properties the instantly claimed subject matter would have.

It is known for biomolecules such as nucleic acids and proteins that single nucleotide or amino acid changes in a given sequence can completely alter or destroy the function of the biomolecule, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and, therefore, unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule

of known function and therefore lacks support regarding utility and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Attwood, T. [Science Vol. 290, Pages 471-473, (Oct. 2000)]; Gerhold et al.[BioEssays, Volume 18, Number 12, pages 973-981{1996)]; Wells et al.[Journal of Leukocyte Biology, Volume 61, Number 5, pages 545-550 (1997)]; and Russell et al.[Journal of Molecular Biology, Volume 244, pages 332-350 (1994)].

Claims 1, 11-13, 15-22, 24, 28, 30, and 31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

B. Claim Rejections under 35 U.S.C. 112, First Paragraph

Claims 1, 22, 24, and 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the

application was filed, had possession of the claimed invention. This rejection is maintained from the Office action mailed 04/12/2004.

The specification discloses SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 which putatively encode various phosphogluconate pathway enzymes. Claims 1, 22, 24 and 28 are drawn to an isolated nucleic acid molecule that encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof. The instant disclosure does not teach or disclose any open reading frames (ORFs) that are contained within SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 such that a maize or soybean phosphogluconate pathway enzyme or fragment thereof would be obtained by expression of an isolated nucleic acid molecule as instantly claimed. Therefore, one of skill in the art would not recognize that applicants were in possession of a purified nucleic acid molecule that encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof as instantly claimed. It is further noted, that instant claims 11-13, 15-22, 30, and 31 drawn to a substantially purified nucleic acid molecule consisting of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569 and 619 or complement thereof meet the written description provision of 35 USC 112, first paragraph.

Claims 1, 22, 24, and 28 are rejected under U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. This rejection is maintained from the Office action mailed 04/12/2004.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

The instant claims are not enabled because neither the specification nor the prior art teach how to make the claimed enzymes from the SEQ ID NO's recited. Table A of the specification discloses that the claimed nucleic acid sequences encode the recited enzymes; however, it is again noted that homology alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence. The instant specification does not disclose anywhere that the claimed nucleic acids actually encode any peptide or protein. While the prior art teaches isolated nucleic acid sequences which encode plant enzymes similar to those recited in the claims, the sequences taught by the prior art are not the same as those recited in the instant claims. As set forth above, each nucleic acid claimed comprises several ATG codons, any of which may be a possible start site for translation into a peptide, but no ORF has been disclosed as that encoding the claimed protein. It is known in the art that nucleic acids (genes) from eukaryotic organisms often comprise multiple open reading frames, (i.e. multiple start and/or stop codons), therefore one skilled in the art to must determine, for any given sequence, which open reading frame to use to generate a peptide. Given an amino acid sequence for a particular peptide, it would require fairly routine

experimentation to "line up" the encoding polynucleotide with the peptide sequence to determine which portion of the nucleic acid sequence comprises the coding region for the peptide. The instant specification does not disclose any amino acids sequences. As no information which would allow one skilled in the art to determine how to generate the specific peptides used for the homology comparisons of Table A of the instant specification, it would require undue experimentation for one skilled in the art to determine how to generate the peptides, with the functionality claimed, from the disclosed nucleic acid sequences. The specification does not disclose or point to information with regard to activity assays, which would also be necessary to determine if any expressed protein actually IS the enzyme recited.

The skilled practitioner would first turn to the instant specification for guidance in using the claimed invention. However, the disclosure lacks clear evidence that the instantly claimed nucleic acid molecules actually encode encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not teach that the nucleic acid sequences as instantly claimed encode any known encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof. Finally, said practitioner would turn to trial and error experimentation to determine how to make a maize or soybean phosphogluconate pathway enzyme or fragment using the instantly claimed purified nucleic acid molecules. Such amounts to undue experimentation.

(10) Response to Argument

In regard to the rejection of claims 1, 11-13, 15-22, 24, 28, 30, and 31 under 35 USC § 101 because the claimed invention lacks patentable utility, appellants argue that nucleic acid sequences are shown in the specification to correlate to genes of known function and proteins involved in the phosphogluconate pathway (see Appeal Brief, page 6, lines 14-18). Appellants further argue that the specification discloses a specific and substantial use for the claimed nucleic acid molecules in identifying polymorphisms related to the recited phosphogluconate pathway enzyme (see Appeal Brief, page 6, lines 18-21.

In response, it is maintained that absent additional factual evidence, teaching a percentage similarity of less than 100% between a given sequence and a known sequence that encodes a protein of known function does not provide sufficient guidance or support to one skilled in the art so as to determine what biochemical activity or properties the instantly claimed subject matter would have. It is further reiterated that it is known for biomolecules such as nucleic acids and proteins that single nucleotide or amino acid changes in a given sequence can completely alter or destroy the function of the biomolecule, albeit not in all cases. The effects of these changes are largely unpredictable as to which sequence alterations may or may not have a significant effect on biological function. Therefore, the disclosure of sequence similarities set forth in Table A of the instant disclosure provides an unpredictable and, therefore, unreliable correspondence between the claimed nucleic acid molecules and known sequences involved in the phosphogluconate pathway.

Several publications are cited in support of the unpredictable relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Attwood, T. [Science Vol. 290, Pages 471-473, (Oct. 2000)]; Gerhold et al.[BioEssays, Volume 18, Number 12, pages 973-981{1996)]; Wells et al.[Journal of Leukocyte Biology, Volume 61, Number 5, pages 545-550 (1997)]; and Russell et al.[Journal of Molecular Biology, Volume 244, pages 332-350 (1994)]. Applicants arguments do not address the teachings of the cited prior art.

Appellants further argue that the specification as filed provides correlations between the claimed nucleic acid molecules and the well known phosphogluconate pathway enzymes as supported by the identities set forth in Table A of the specification (see Appeal Brief, page 7, lines 18-21). Appellants further argue that a rigorous correlation need not be provided in order to establish practical utility, reasonable correlation is sufficient and cite *Fujikawa v. Wattanasin* (Fed. Cir. 1996) as support (see Appeal Brief, page 7, line 22 through page 8, line 6 and page 8, lines 8-14).

In response, it is reiterated that absent additional factual evidence, teaching a percentage similarity of less than 100% between a given sequence and a known sequence that encodes a protein of known function does not provide sufficient guidance

or support to one skilled in the art so as to determine what biochemical activity or properties the instantly claimed subject matter would have.

Appellants further argue that the Vosnidou Declaration (filed 04/24/2006) provides additional evidence that SEQ ID NO: 1 has 95 percent identity to a gene that is similar to one which encodes a glucose-6-phosphate 1-dehydrogenase (see page 8, lines 6-8). It is noted that the Vosnidou Declaration, filed 04/24/2006, asserts that a computer search was conducted using a BLASTN query of SEQ ID NO: 1 and the results indicated a 95% identity to GenBank Accession No 60672339, identified as similar to a glucose-6-phosphate dehydrogenase.

In response, it is first noted that the BLASTN search performed on SEQ ID NO: 1 was not disclosed in the instant application at the time of filing and serves to demonstrate that nucleic acid molecules as instantly claimed require further research to establish a specific and substantial utility. Additionally, the sequence identified by GenBank Accession No 60672339 is indicated only as encoding a protein similar to a glucose-6-phosphate dehydrogenase. However, there is no indication that the sequence identified by GenBank Accession No 60672339 actually encodes a protein which is a glucose-6-phosphate dehydrogenase, and thus fails to establish any known biological function associated with said sequence. Further, 95% sequence identity between SEQ ID NO: 1 and the sequence identified by GenBank Accession No 60672339 does not provide sufficient evidence, guidance, or support to one skilled in the art so as to

determine what biochemical activity or properties the instantly claimed subject matter would have.

Appellants further argue that the utilities of SEQ ID NOs are specific because they are specific to the claimed SEQ ID NOs and not generally applicable to any nucleic acid sequence. Appellants further ague this utility is substantial and credible because SEQ ID NO:1 can be used to isolate genes, map genes, and determine gene function with a maize glucose-6-phosphate 1-dehydrogenase enzyme (see Appeal Brief, page 8, lines 15 through page 9, line 9).

In response, it is maintained that nucleic acid molecules used to isolate genes, map genes, and determine gene function with a maize glucose-6-phosphate 1-dehydrogenase enzyme is a general utility of a any sequence from the large genus of nucleic acid sequences that share any degree of sequence identity with a gene encoding a maize glucose-6-phosphate 1-dehydrogenase enzyme or, further, to any gene in the phosphogluconate pathway as instantly claimed. Such uses are not specific to the nucleic acid molecules as instantly claimed. Further, such uses are not substantial as isolating genes, mapping genes, and determining gene function provide only an invitation for further research. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved is not a substantial utility.

In regard to a nucleic acid having utility based on a peptide activity that must be known or established, appellants further argue that the activity of all enzymes are known to one of ordinary skill in the art and that any standard biochemistry textbook discloses the activities of the recited phosphogluconate pathway enzymes (see Appeal Brief, page 9, line 20 through page 10, line 13).

In response, it is maintained that the instant disclosure does not provide sufficient evidence or guidance such that one of ordinary skill in the art would recognize that the nucleic acid molecules as instantly claimed actually encode a protein or, further, encode proteins involved in phosphogluconate pathway enzymes as instantly claimed. It is reiterated that teaching a percentage similarity of less than 100% between a given sequence and a known sequence that encodes a protein of known function does not provide sufficient guidance or support to one skilled in the art so as to determine what biochemical activity or properties are possessed by the instantly claimed subject matter.

Appellants further argue that by setting forth a reasonable correlation between the claimed nucleic acid molecules and known enzymes, the specification need not contain examples of actual activity if the invention is otherwise disclosed in a such a manner that one of skill in the at would be able to practice it without undue amount of experimentation (see page Appeal Brief 10, lines 14-22).

In response, it is reiterated that the instant specification only discloses percent identity between the instantly claimed nucleic acid molecules and known sequences involved in the phosphogluconate pathway enzymes. No further evidence is disclosed

that confirms a real world biological activity or function associated with the nucleic acid molecules as instantly claimed. The instant rejection relies upon several publications to demonstrate the unpredictable relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research (see Attwood, T. [Science Vol. 290, Pages 471-473, (Oct. 2000)]; Gerhold et al.[BioEssays, Volume 18, Number 12, pages 973-981{1996)]; Wells et al.[Journal of Leukocyte Biology, Volume 61, Number 5, pages 545-550 (1997)]; and Russell et al.[Journal of Molecular Biology, Volume 244, pages 332-350 (1994)].) Therefore, one of skill in the art would not be able to practice or use the claimed invention based on the instant disclosure due to the unpredictable relationship between sequence and function as demonstrated by the cited art.

In regard to both the rejection of claims 1, 11-13, 15-22, 24, 28, 30, and 31 under 35 U.S.C. § 112, first paragraph, specifically because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility, such that one skilled in the art would not know how to use the claimed invention, and the rejection of claims 1, 22, 24, and 28 under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement, Appellants argue that that the specification provides considerable direction and guidance and have presented working examples such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation (see Appeal Brief, page 11, line 4 through page 13, line 19).

In response, it is maintained that the instant specification fails to provide sufficient direction, guidance, or working examples that support either a specific and substantial asserted utility or a well established utility.

In regard to the rejection of claims 1, 22, 24, and 28 under 112, First paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, appellants argue that they have disclosed common structural features of the claimed SEQ ID NOs and modification thereof and, therefore, have satisfied the written description requirement.

In response, it is noted that the common structural features of the claimed SEQ ID NOs disclosed in the instant specification amount to a listing of percent identities between said SEQ ID NOs and sequences involved in the phosphogluconate pathway. It is maintained that sequence identity alone is insufficient to reliably establish a phosphogluconate activity for any protein that may be encoded by the nucleic acid molecules as instantly claimed.

Appellants further argue that the Examiner has offered no evidence to demonstrate, in light of Appellants disclosure, why one of ordinary skill in the art would reasonably doubt that the invention encompassed by the claims have not been adequately described in the present disclosure.

In response, it is noted that the instant rejection relies upon several publications to demonstrate the unpredictable relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research (see Attwood, T. [Science Vol. 290, Pages 471-473, (Oct. 2000)]; Gerhold et al.[BioEssays, Volume 18, Number 12, pages 973-981{1996)]; Wells et al.[Journal of Leukocyte Biology, Volume 61, Number 5, pages 545-550 (1997)]; and Russell et al.[Journal of Molecular Biology, Volume 244, pages 332-350 (1994)].)

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Eric DeJong

Examiner 09/27/2007

Conferees:

Marjorie Moran

Supervisory Patent Examiner

SPE, 1631

Ram Shukla

Supervisory Patent Examiner

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER